PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Ullrich, A. *et al.*

Serial No.: 08/426,509 Group Art Unit: 1646

Filed: April 21, 1995 Examiner: Sally Teng

For: NOVEL MEGAKARYOCYTIC PROTEIN TYROSINE KINASES Attorney Docket No.: 7683-074

SECOND DECLARATION OF AXEL ULLRICH, MIKHAIL GISHIZKY, AND IRMIGARD SURES UNDER 37 CFR § 1.131

Assistant Commissioner for Patents
Washington, D.C. 20231

We, Axel Ullrich, Ph.D., who resides at Adalbertstr. 108, 80798 München, Germany, Mikhail Gishizky, Ph.D., who resides at 3001 B. Bryant Street, Palo Alto, California, and Irmigard Sures, Ph.D., who resides at Forstenrieder, Allee 55, 8000 München, Germany, do declare that:

1. We are the co-inventors of the presently claimed invention in the above-identified application.

2. The above-identified patent application relates to the isolation and characterization of novel non-receptor tyrosine kinase proteins from megakaryocytes, which are referred to as MKK1, MKK2, and MKK3. These proteins are characterized by an intracellular tyrosine kinase domain, a SH2 src homology domain, and a SH3 src homology domain.

3. Attached hereto is a copy of the Declaration of AXEL ULLRICH, MIKHAIL GISHIZKY and IRMIGARD SURES Under 37 CFR § 1.131 filed in co-pending

application Serial No. 08/232,545 (the parent of the instant application). This Declaration includes Exhibits A through D identified as follows:

(A) Exhibit A is a printout of an electronic mail message from Jeanne Arch in Germany to her account at SUGEN in the United States, in which she transmitted the complete sequence of MKK1. Jeanne Arch is the personal assistant of inventor Axel Ullrich. Although the date when the electronic mail message was transmitted to the United States which follows the heading "Date:", is redacted, this date is prior to January 14, 1994.

(B) Exhibit B is a printout of an electronic mail message from Jeanne Arch in Germany to her account at SUGEN in the United States, in which she transmitted the complete sequence of MKK3. Although the date when the electronic mail message was transmitted to the United States which follows the heading "Date:", is redacted, this date is prior to August 5, 1993.

(C) Exhibit C is a page copied from the laboratory notebook of Brad Yatabe documenting work performed under the direction and control of inventor Mikhail Gishizky using the MKK1 clone at SUGEN, Inc. in the United States.

(D) Exhibit D is a page copied from the laboratory notebook of Brad Yatabe documenting work performed under the direction and control of inventor Mikhail Gishizky using the MKK3 clone at SUGEN, Inc. in the United States.

4. For the purposes of executing this declaration, we have again reviewed the documents of Exhibits B and D. Although we have redacted the dates to preserve confidentiality, the document in Exhibit B was dated prior to August 5, 1993, while the document in Exhibit D was dated prior to January 14, 1994. Although the work described below in Paragraphs 5, 6, and 7 was performed outside the United States, we hereby confirm that the act relied upon and described in Paragraph 8, i.e. introduction of the invention into the United States, was carried out prior to August 5, 1993.

5. Prior to August 5, 1993, we successfully identified three PCR fragments encoding a portion of three different novel non-receptor tyrosine kinases, referred to as MKK1, MKK2, and MKK3, as exemplified in the above-identified patent application at

p. 37, line 12 to p. 38, line 27. Specifically, a cDNA library was generated using total RNA prepared from the human megakaryocytic cell line K-562. Two pools of degenerate primers were designed on the basis of highly conserved sequences within the kinase domain of receptor tyrosine kinases corresponding to the amino acid sequence HRDLAA and SDVWSF/Y. These primers were used in a polymerase chain reaction with the K-562 cDNA as a template. The products of the polymerase chain reaction were subjected to polyacrylamide gel electrophoresis and fragments of the expected size isolated and subcloned into pBluescript. After sequencing many of these subcloned PCR fragments, three different clones, MKK1, MKK2, and MKK3, were identified that derived from novel tyrosine kinases.

6. Prior to August 5, 1993, we conceived the idea that the PCR fragment could be used to screen cDNA libraries prepared from human fetal brain and human placenta to identify and clone a full-length cDNA encoding each of the MKK's. For each MKK identified above, the novel PCR clone was radioactively labeled as used as a probe to screen bacteriophage libraries prepared from human fetal brain and human placental cDNA.

7. Prior to August 5, 1993, we successfully cloned full length cDNA's encoding MKK1, MKK2, and MKK3, using this strategy, as disclosed and exemplified in the above-identified application at p. 37, line 12 through p. 39, line 20.

8. Prior to August 5, 1993, we had transmitted on our behalf the complete sequence of the full length cDNA clone of MKK3 to SUGEN, Inc., the assignee of the above-identified application, at that time located in Redwood City, California, U.S.A., as shown in the electronic mail message of Exhibit B. Jeanne Arch, the personal assistant of inventor Axel Ullrich, was the author of this message. Exhibit B, containing the message entitled "Subject: MKK3-FIN.SEQ", conveyed the sequence of a full length clone of MKK3. The sequence MKK3-Fin.Seq shown in Exhibit B corresponds to the sequence of MKK3 in Figure 3A and 3B as originally filed in the above captioned application. The sequence of the MKK3 clone was independently confirmed in the United States at SUGEN, Inc.

9. I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of United States Code and that such willful false statements may jeopardize the validity of the application of any patent issuing thereon.

DATED: 12-10-99

Axel Ullrich

DATED: 12-10-99

Irmigard Sures

DATED: 11-24-99

~~Mikhail~~ Gishizky